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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,164	12/20/2001	Benjamin J. Metcalf	33,484-00	3977

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EXAMINER

DUFFY, PATRICIA ANN

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/019,164

Applicant(s)

METCALF, BENJAMIN J.

Examiner

Patricia A. Duffy

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## RESPONSE TO AMENDMENT

The amendment filed 2-25-04 has been entered into the record. Claims 9-17 have been cancelled. Claims 1-8 are pending and examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

### *Objections/Rejections Withdrawn*

The notation of the priority information in the first line of the specification is acknowledged. It is also noted that the claim for priority was presented in the declaration/oath as originally filed and is therefore timely.

### *Rejections Maintained*

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the term "a tightly regulated promoter". The term "tightly" is a measure of degree and comparison and neither the art nor the specification define the term as it relates to any other promoter. For example, if all promoters were not in some fashion regulated then all genes would be expressed all the time. Therefore, all promoters appear to be regulated in nature. The specification does not define "tightly regulated promoters" and does not teach the specific features of these promoters, such that the skilled artisan would be able to readily distinguish any regulated/inducible promoter of the art from those that are "tightly regulated".

Applicants argue the function of a tightly regulated promoters function set forth on page 12, lines 10-30 as one that down regulates the production of a recombinant PAL mRNA under specific conditions and that tight regulation can be removed under specific

conditions to allow for maximized recombinant protein production and these are distinguished from promoters which are allegedly not under tight transcriptional regulation. This is not persuasive, the lac operon promoter would fall under the definition of tightly regulated promoter, down regulating the production of a recombinant protein in the absence of lactose and upregulating the production of the protein when lactose is present. However, Applicants argue that promoters such as "lac" are not "tightly regulated", however it is noted that the lac promoters fit the definition of tightly regulated on page 12, lines 10-30. The fact that "lac" is "leaky" does not distinguish lac from the "tightly regulated promoter" as apparently functionally defined at page 12 and argued by Applicants. As such, the allegedly leaky promoters meet the functionality of Applicants' own cited passage and makes it clear that no definition of "tightly" regulated promoter is set forth in the specification because the allegedly functionally similarly regulated promoters, such as lac, that clearly meet the definition of page 12 are considered by Applicant to be not under tight regulation (page 3, lines 29-35). The definition on page 12 is inconsistent with the known function of the lac promoter in regards to down regulation in the absence and upregulation in the presence of lactose (i.e. the specific conditions recited at page 12). Applicants asserted definition of "tightly regulated" promoters does not provide for the metes and bounds of "tightly regulated" because it is a term of comparison and the asserted definition in the specification is internally inconsistent. As such, one skilled in the art would be unable to ascertain the metes and bounds of a "tightly regulated promoter".

Applicants have not addressed the issue of: "Further, it is noted that DNA can not be expressed in lipidated form and this limitation is not interpretable."

Claims 1, 2 and 8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Anilionis et al (WO 90/02557, published 22 March 1990) in light of Nelson et al (Infection and Immunity, 56(1):128-134, 1988) is maintained for reasons made of record..

Applicants arguments have been carefully considered but are not persuasive to remove the rejection. Applicants argue that Anilionis et al does not teach a tightly regulated promoter because "lac" is a leaky promoter because it has some level of protein expression in the absence of inducer. This is not persuasive, Applicants asserted definition is that one that down regulates the production of a recombinant PAL mRNA under specific conditions and that tight regulation can be removed under specific conditions to allow for recombinant protein production. The lac promoter clearly fits this asserted criteria. The asserted requirement for the absence of transcription in the absence of inducer is not that which is allegedly defined by the specification and relied upon by Applicants.

Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anilionis et al (WO 90/02557, published 22 March 1990) in light of Nelson et al (Infection and Immunity, 56(1):128-134, 1988) as applied to claims above 1, 2 and 8, and in view of Guzman et al (Journal of Bacteriology, 177(14):4121-4130, 1995) is maintained for reasons made of record.

Claims 3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anilionis et al (WO 90/02557, published 22 March 1990) in light of Nelson et al (Infection and Immunity, 56(1):128-134, 1988) as applied to claims above 1, 2 and 8, and in view of Mertens et al (Gene, 164:9-15, 1995) is maintained for reasons made of record.

Claims 3, 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anilionis et al (WO 90/02557, published 22 March 1990) in light of Nelson et al (Infection and Immunity, 56(1):128-134, 1988) as applied to claims above 1, 2 and 8, and in view of Mertens et al (Gene, 164:9-15, 1995) and Novagen Inc., admittedly commercially available in specification page 15, line 34) is maintained for reasons made of record.

Inasmuch as, the 103 rejections have been traversed together they will be rebutted together. Applicants argue that none of Anilionis et al promoters are tightly regulated promoters. This is not persuasive for reasons made of record for claim 1, 2 and 8 supra. Applicants reiterate the teachings of record and acknowledges that all the limitations have been met. Applicants argue that most if not all inventions arise from a combination of old elements and that identification in the prior art of the limitation is insufficient to defeat patentability of the whole claimed invention and that this is hindsight reconstruction. In response to Applicants' argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, motivation was clearly articulated in Anilionis et al and relied upon by the examiner. Anilionis et al clearly directed one toward bacterial host cell strains and expression vectors may be chosen which inhibit action of the promoter unless induced (page 29, lines 27-30) and for purposes of expression of a cloned gene, it is also desirable to use strong promoters in order to obtain a high level of transcription (page 29, line 10-15). There is explicit motivation in the article to use any of the promoters of Guzman et al, Mertens/Novagen because they fulfill the requirements set by Anilionis et al. (i.e. regulatable and strong promoters). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir.

1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a clear teaching is present in Anilionis et al. Applicants are incorrect in that no evidence or suggestion is found in the art. Applicants argue that all indicia of nonobviousness must be considered when assessing patentability and indicate that several laboratories were unable to express lipidated rP6 in large quantities. This is not persuasive because it is not a teaching away. Expression of lipidated rP6 was possible and was performed by the art and is acknowledged in Applicants response. Applicants argue that the inability to "overexpress" would teach away from using other systems. This is not persuasive, there is a clear motivation to use regulated promoters and strong promoters as set forth in Anilionis et al to obtain a high level of transcription. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Further, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991) (discussed below). Although *Ex parte Levengood*, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done" (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. The motivation clearly resides in Anilionis et al to use inducible promoters and further strong promoters to achieve a high level of transcription. As such, the prior art specifically points one to the prior art for additional systems. Moreover, Applicants acknowledge that Anilionis et al

produces low levels of PBOMP-1. It is further noted that only expression is required and that this is a property of the vector in a host cell and not a property of the claimed plasmid per se. Applicants are arguing limitations not set forth in the specification and further, the high levels of expression are suggested by the art as combined.

The rejection is maintained.

#### *Status of Claims*

Claims 1-8 stand rejected.

#### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

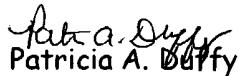
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Art Unit: 1645

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 6:30 pm - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

  
Patricia A. Duffy

Primary Examiner

Art Unit 1645